

**REMARKS**

**Status of the Claims**

Claims 1, 3 and 5-20 are now pending in the application. In the present Amendment, claims 1, 6, 8, 11 and 12 have been amended. Support for these amended claims can be found throughout the specification and the originally filed claims. Applicants have not introduced any new matter by the amendments.

Specifically, support for the language “pre-treating the sample to enable amplification of nucleic acids contained in the sample” can be found, *inter alia*, at page 43, line 19, to page 44, line 14, of the specification.

Support for the contents of the kits recited in amended claims 11 and 12 can be found, *inter alia*, at page 31, line 21, to page 34, line 4, of the specification.

**Rejections Under 35 U.S.C. § 112, Second Paragraph**

Claims 1 and 3 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for reciting the term “exposing.” Claim 1, claim 3 dependent therefrom, has been amended to recite “pre-treating the sample to enable amplification of nucleic acids contained in the sample” to clarify the step of exposing the nucleic acids.

Claims 6 and 8 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for using the past and present tense to define the determining step. Claims 6 and 8 have been amended to clarify that the PCR-amplified and labeled nucleic acids are used as probes for complementary hybridization with known gene fragments or as probes for a DNA microarray.

Claim 7 was rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for reciting the term “the known gene fragments.” According to the Office, it is

unclear if the known gene fragments are the actual probes or something different.

Claim 6, from which claim 7 depends, has been amended to clarify that the nucleic acids amplified and labeled by the method of claim 5 are subsequently used as probes to hybridize with known gene fragments. Accordingly, Applicants submit that claim 7 clearly recites that the known gene fragments are not hypothetical, but rather are any known gene fragment complementary to the PCR-amplified and labeled probes.

Claims 11-18 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for not specifying the contents of the claimed kits. Claims 11 and 12, from which claims 13-18 depend, have been amended to recite that the kits comprise a support divided into a plurality of compartments.

In view of the claim amendments and arguments presented above, Applicants respectfully request that all rejections under 35 U.S.C. § 112, second paragraph, be withdrawn.

#### **Rejections Under 35 U.S.C. § 102(e)**

Claims 1, 3, 9-10 and 19 were rejected under 35 U.S.C. § 102(e) as being anticipated by Chu (U.S. Patent No. 6,703,247). Applicants respectfully traverse.

A *prima facie* case of anticipation requires that a single publication teach, either expressly or inherently, each and every element or limitation of the claim, including any functional limitations. M.P.E.P. § 2131. According to the Office, Chu teaches fixing a cell-containing sample in divided compartments of a support and placing a PCR mixture into the compartments of the support. Office Action, page 5. Applicants respectfully submit that neither of these claim elements are disclosed or suggested by Chu.

Applicants thus submit that Chu does not anticipate claims 1, 3, 9-10 and 19.

Chu, at best, discloses the fixation of cell samples to slides, which may in turn be placed in other vessels for further analyses. For example, the slides may be placed in a “multislide holder” for microscopic analysis of multiple slides (see col. 2, lines 34-40, as referred to by the Examiner). Alternatively, the multislide holder containing attached slides may be placed into “a specially designed in situ PCR aluminum tray” that contains PCR reagents (see Example 4, col. 24, lines 19-64).

Chu does not disclose or suggest a support having divided compartments in which cell-containing samples are fixed, as recited directly or indirectly in claims 1, 3, 9-10 and 19. Further, Chu does not teach or suggest placing a PCR mixture into these same divided compartments within the support, as also recited directly or indirectly in claims 1, 3, 9-10 and 19.

Thus, for at least the reasons discussed above, Chu does not disclose or suggest each and every element of claims 1, 3, 9-10 and 19. Accordingly, Chu does not anticipate claims 1, 3, 9-10 and 19, and Applicants respectfully request that this rejection be withdrawn.

#### **Rejections Under 35 U.S.C. § 102(b)**

Claims 1, 3, 9-17 and 19 were rejected under 35 U.S.C. § 102(b) as being anticipated by Cloyd et al. (U.S. Patent No. 6,448,014). Claims 1, 3, 5-6, 9-10 and 19-20 were also rejected under 35 U.S.C. § 102(b) as being anticipated by Blumenfeld et al. (U.S. Patent No. 6,228,634). Because neither Cloyd et al. nor Blumenfeld et al. teach each and every element of the pending claims, Applicants respectfully traverse.

According to the Office, Cloyd et al., at Example 2, teaches fixing a cell-containing sample in divided compartments of a support and placing a PCR mixture into

the compartments of the support. Office Action, page 6. However, Example 2 of Cloyd et al. specifically states that the cell samples were cytocentrifuged onto glass slides, which are then dipped into paraformaldehyde to fix the cells. Cloyd et al. thus discloses fixing individual cell samples to a single support. A PCR reaction is then carried out on each individual slide. Cloyd et al. does not teach or suggest a support with divided compartments, fixing a cell-containing sample to such a support, or placing a PCR mixture into the compartments of the support.

The Office also asserts that Blumenfeld et al. discloses fixing a cell-containing sample in divided compartments of a support and placing a PCR mixture into the compartments of the support. Office Action, page 7. Blumenfeld et al., however, simply teaches, at best, PCR methods for cells samples fixed on individual microscope slides. For example, col. 17, lines 46-55, states that “a biological sample, such as a histochemical section or cytochemical smear attached to a microscope slide” is covered with a PCR reagent mixture and then “the microscope slide is placed on a ceramic thermal cycler sample plate.”

In short, Blumenfeld et al. discloses PCR methods for individual biological samples fixed on individual slides. Blumenfeld et al. does not teach or suggest a support with divided compartments, fixing a cell-containing sample to such a support, or placing a PCR mixture into the compartments of the support.

As with Chu, neither Cloyd et al. nor Blumenfeld et al. disclose or suggest each and every element of the pending claims. Thus, Cloyd et al. does not anticipate claims 1, 3, 9-17 and 19, and Blumenfeld et al. does not anticipate claims 1, 3, 5-6, 9-10 and 19-20.

Claims 11-17 were rejected under 35 U.S.C. § 102(b) as being anticipated by Krystosek et al. (U.S. Patent No. 5,264,343) and, alternatively, by Saunders (U.S. Patent No. 6,087,134). According to the Office, although neither reference teaches a kit according to the specific uses recited in claims 13-17, the references teach a kit useful for practicing the methods recited in claims 1 and 10. Because the Office has found claims 11-17 indefinite for not reciting the contents of the claimed kits, the Office thus concludes that Krystosek et al. and Saunders anticipate claims 11-17. Applicants respectfully traverse.

Claims 11 and 12 have been amended to recite kits that comprise a support divided into a plurality of compartments. Claims 13-17 depend from claims 11 and 12, and therefore indirectly recite this claim element. Krystosek et al. and Saunders do not disclose or suggest kits that comprise a support divided into a plurality of compartments, and thus do not anticipate claims 11-17.

Krystosek et al. discloses methods of detecting the presence or absence of exposed nuclear DNA. The Office asserts that col. 10, lines 34-58, and claims 13-20 of Krystosek et al. disclose kits useful for practicing the invention of claims 1 and 10. Office Action, page 8. The sections referred to by the Office, however, merely disclose basic PCR kits comprising DNA polymerase I, nucleotides, detecting means, and a slide of fixed cells. Krystosek et al. does not teach or suggest a kit containing a support divided into a plurality of compartments.

Saunders discloses methods for analyzing cellular DNA. Unlike the present invention, however, cell samples are deposited on individual slides prior to further manipulations (see, for example, Figure 1). Saunders simply does not disclose or even

suggest a support with divided compartments, let alone fixing a cell-containing sample to such a support, or placing a PCR mixture into the compartments of the support.

Because neither Krystosek et al. nor Saunders disclose or suggest each and every element of claims 11-17, as amended, the references do not anticipate claims 11-17.

Thus, for at least the reasons discussed above, Cloyd et al., Blumenfeld et al., Krystosek et al., and Saunders do not anticipate the amended claims. Accordingly, Applicants respectfully request that all rejections under 35 U.S.C. § 102(b) be withdrawn.

#### **Rejection Under 35 U.S.C. § 103(a)**

Claims 7-8 were rejected under 35 U.S.C. § 103(a) as obvious over Blumenfeld et al. in view of Stapleton et al. (U.S. Patent No. 6,103,192). Claim 18 was rejected under 35 U.S.C. § 103(a) as obvious over Krystosek et al. in view of Saunders. Because neither Blumenfeld et al. nor Krystosek et al., whether considered alone or in combination with Stapleton et al. or Saunders, teach each and every element of claims 7-8 or 18, Applicants respectfully traverse.

A *prima facie* case of obviousness has three distinct requirements. First, the references must teach or suggest every claim element. M.P.E.P. §§ 2142 and 2143.03. Second, there must be a motivation to modify or combine the teachings of the cited references. M.P.E.P. §§ 2143 and 2143.01. Third, there must be a reasonable expectation of success in performing the modified or combined teachings of the references. M.P.E.P. § 2143.02.

Claims 7-8 and 18 each indirectly recite fixing a cell-containing sample in divided compartments of a support and placing a PCR mixture into the compartments of the support. As discussed above, Blumenfeld et al., Krystosek et al., and Saunders do not teach or suggest these claim elements. Likewise, Stapleton et al. does not compensate for the deficiencies of Blumenfeld et al.

Stapleton et al. discloses a method for collecting biological samples. As recognized by the Office, the method of Stapleton et al. (specifically, Example 5 at col. 22) involves immobilizing cells on a nylon matrix and then applying aliquots of the matrix to individual tubes for further analyses, including amplification. Stapleton et al., however, does not teach or suggest a support with divided compartments, fixing a cell-containing sample to such a support, or placing a PCR mixture into the compartments of the support.

Therefore, even combining the teachings of Blumenfeld et al. and Stapleton et al. or Krystosek et al. and Saunders, one does not arrive at the claimed invention. Because none of these references, alone or combined, teach each and every element of claims 7-8 or 18, Applicants submit that claims 7-8 and 18 are patentable over the cited references. Applicants thus respectfully request that all rejections under 35 U.S.C. § 103(a) be withdrawn.

## **Conclusions**

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance

of the pending claims. If the Examiner has any questions regarding this Amendment and Response, the Examiner is invited to contact the undersigned at 303-863-9700.

In the event that any fees are due in connection with this response, please debit Deposit Account No. 19-1970.

Respectfully submitted,

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